Medicare Participating Heart Bypass Center Demonstration:

Appropriateness Study - Indications for Coronary Artery Bypass Graft Surgery

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I. INTRODUCTION

The accepted indications for coronary artery bypass grafting (CABG) have been evolving since the introduction of this technique. Most commonly-used guidelines were developed in the early 1980s and incorporate the results of several large randomized clinical trials which had been performed during the 1970's. The treatment of coronary artery disease (CAD), however, has been undergoing constant evolution during the more than twenty years since these trials were performed. Improvements in the technique of coronary artery bypass surgery (such as crystalloid cardioplegia and routine use of internal mammary grafts), the introduction of percutaneous transluminal coronary angioplasty (PTCA) and the development of new pharmacologic entities (especially calcium channel antagonists and thrombolytics) have had a profound effect on the management of patients with coronary artery disease. These developments have resulted in important changes in the way CABG is being and should be used. This paper will attempt to identify these changes and provide information required for the development of a consensus on appropriate indications for CABG among patients involved in the Health Care Financing Administration's (HCFA) Medicare Participating Heart Bypass Demonstration program. Particular attention will be directed toward PTCA, a treatment modality that has resulted in changes in the way in which CABG is used, and on internal mammary artery grafting, a technique that might have significant effects on interpreting the results of early studies of long-term survival of patients undergoing CABG.

II. APPROACH

In 1986, Chassin and his colleagues at the Rand Corporation reviewed the medical literature and published a listing of indications for CABG. This publication, based on the results of clinical trials performed during the 1970s, provides the starting point for review of

the current indications for CABG. We will present the indications as recommended by RAND (summarized in Appendix A) and then discuss issues that may limit their applicability both in general and specifically to patients enrolled in the Medicare demonstration.

In developing their indications for CABG, researchers at the Rand Corporation reviewed 185 reports on CABG in the medical literature. Three large randomized clinical trials (RCTs), the Veterans Administration Cooperative Study (VACS), the European Coronary Surgery Study (ECSS) and the Coronary Artery Surgical Study (CASS), were especially influential in determining the indications for CABG. These studies, performed in the 1970s, were the only large RCTs available for consideration. This continues to be the case. Since Rand reviewed the literature there has been further follow-up of these three studies and a large number of reports from uncontrolled clinical studies; however, there have been no new large RCTs.

Changes in indications for CABG surgery since that time may result from the development of new technologies (especially PTCA) that may have supplanted CABG as the preferred intervention in certain situations and the effects of changes in medical or surgical technique that alter the outcomes data of the early studies of CABG in such a way as to alter the relative effectiveness of medical or surgical treatment.

A. Chronic Stable Angina

The efficacy of CABG at providing symptomatic relief for anginal symptoms has long been recognized. CASS, ECSS, VACS and smaller studies (including those performed in Houston, Seattle and Oregon) all demonstrated the ability of CABG to relieve angina.

However, since these studies were performed there has been considerable improvement in medical therapy for angina. The introduction of long acting and more specific beta-blockers, improvements in long and short acting nitrates, and the introduction of calcium channel blockers have all strengthened the non-invasive armamentarium for treatment of angina pectoris. In addition, the introduction of PTCA in 1977 and its continued refinement provides an important competitor to CABG for the treatment of chronic stable angina (CSA).

Consequently the relevant question to be addressed when considering the use of CABG for treatment of CSA is whether surgical intervention results in improved mortality and symptom relief relative to medical treatment or PTCA. The evidence on this is mixed and appears to depend upon the anatomical extent of CAD.

1. Left Main Disease

The VACS demonstrated a clear advantage to surgery in the treatment of left main disease (Detre, et al., 1977). Indeed, this finding was so readily accepted that the European study made inclusion of patients with left main disease optional. CASS excluded patients with left main disease altogether from randomization. After seven year follow-up, patients in the VACS with left main disease in association with other clinical or angiographic cardiac risk factors who were randomized to surgical treatment continued to have a statistically significant improvement in survival (Detre et al. 1985).

The broad acceptance of surgery for left main disease has made a long term study of its effects on mortality impossible. At 11 years, too few patients with left main disease (4 of 48) remained in the medical group to allow for statistically valid comparisons to the surgical

group. Forty-seven percent of the original medical group crossed over to surgery and 44 percent died (Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group 1984).

2. Single and Double Vessel Disease

In contrast to the findings with respect to left main disease, the RCTs fail to demonstrate a survival advantage in patients with single vessel disease and most patients with double vessel disease undergoing CABG.[1] This was true even when patients were stratified by other risk factors.

If there are no survival benefits among patients with single or double vessel disease undergoing surgery, then the role of surgery for this disease is called into serious question. The emergence of angioplasty as a safe and effective means for relieving anginal symptoms in patients with single and double vessel disease (discussed below) and improvements in medical therapy suggest that PTCA or medical management are the preferred modalities for treatment of these lesions.

3. Triple Vessel Disease

The effectiveness of CABG at reducing mortality of patient with triple vessel disease (TVD) is now reasonably well established at least in patients with reduced ventricular function. The ECSS revealed a statistically significant reduction in mortality among patients with TVD undergoing surgery (European Coronary Surgery Study Group 1979, 1980, 1982) while the

[1] There is some question of whether a survival advantage exists among bypass patients with double vessel disease and proximal lesions in the left coronary artery.

VA study and CASS had equivocal results. Initial interpretation of the data from the VA study found no improvement in survival among patients with TVD (Detre et al., 1981), but further analysis of the data suggested some positive effect on mortality for patients undergoing CABG (Takaro et al. 1982). Data from CASS revealed improvement in mortality among some, but not all, subgroups of patients with TVD who underwent CABG. Specifically, the CASS data reveal a statistically significant improvement in mortality among patients with TVD and decreased left ventricular function (manifest by an ejection fraction below 50 percent) (Passamani et al. 1985).

Several factors related to study design may explain these disparate results. First, the different criteria used to select patients for the studies makes the studies not directly comparable. For example:

- Patients needed to have at least 70 percent luminal narrowing to be eligible for CASS while the VACS and ECSS required only a 50 percent narrowing.

- All of the patients in the VACS and ECSS had angina unrelieved by medical therapy, while many of the CASS patients did not. Even among patients with angina, the VACS include patients with class III angina (55 percent) while CASS excluded patients whose angina was greater than class II.

- The VACS and ECSS enrolled only men, while 24 percent of CASS patients were female.

A second factor influencing interpretation of the results of these studies is the variation of surgical mortality rates in the studies. Surgical mortality in the VA study was 5.8 percent. This compares to 3.5 percent in ECSS, 1.4 percent in CASS, and even lower rates in other studies. Although the causes of these differences may include surgical techniques, case mix, or other factors, the net effect of the high mortality rate would be to reduce the benefits of surgery versus medical treatment. Indeed, as noted, Takaro reanalyzed the VA study data and, after exclusion of three hospitals with excessive operative mortality, showed a statistically significant improvement in mortality among patients with TVD who underwent surgery (Takaro et al. 1982). This change in mortality is an important matter for consideration. If the current operative mortality rate is considerably below the rate at the time of the RCTs, then it is possible that surgery now has a more positive impact on long-term survival than indicated by the RCTs and may be preferable to medical treatment in some situations.[2]

Another factor limiting the comparability of the three studies are the differences in time of study performance. Patients were randomized into the VA study between 1972 and 1974, the European study between 1973-1976, and CASS between 1974-1979. Changes in medical treatment and improvements in surgical technique may have had an additional influence on the outcomes of both medical and surgical cohorts.

Long-term follow-up of all three studies reveals that any improvements in mortality of CABG among patients with TVD are lost with time. An 11 year follow-up of the VA study (Detre et al. 1985), 12 year follow-up of the European Study (Varnauskas et al. 1988) and 8

[2] It should be noted, of course, that improvements in medical therapy over the same period could have a similar, but opposite effect.

year follow-up of CASS demonstrate that any advantages of CABG are gradually lost over time (CASS principal investigators 1983, Killip et al. 1985).

B. Unstable Angina

Large randomized clinical trials of the effect of CABG on mortality of patients with unstable angina were lacking at the time of the Rand review. They reviewed four studies (National Cooperative Study, Parkland Study, Portland VA study and Buenos Aires Study) and found significant methodologic problems with each. Although these studies demonstrated that CABG effectively relieved anginal symptoms, the small size of the study populations (27 at Parkland, 43 at Portland VA and 113 in Buenos Aires) made it difficult for small observed differences in mortality to pass tests for statistical significance. A study published since the Rand review suggests that surgical treatment of unstable angina results in no improvement in long-term survival except in select patient groups. Luchi and colleagues at the Veterans Administration (Luchi et al. 1987) randomized 468 men with unstable angina to medical treatment alone or medical treatment plus CABG. Their results, from the period 1976-1982, showed an immediate operative mortality of 4.1 percent but no survival difference at two years except among patients with left ventricular dysfunction (LVEF = 0.30 - 0.59) for whom surgery improved survival. These results suggest that CABG is indicated only in a carefully selected cohort of patients with unstable angina.

C. Following Acute Myocardial Infarction

Even though almost half of the patients enrolled in the three large RCTs had sustained an MI in the past, the Rand review found no studies which looked specifically at whether

there was a difference in outcome among patients who had previously sustained a myocardial infarction (MI). We are aware of no studies published since the Rand review that provide further insight into this question. Although it would be reasonable to presume that the results of the three large RCTs studies apply to patients who develop CSA long after sustaining an MI, the data from these trials may apply to patients developing CSA in the immediate post-infarction period.

D. During Acute Myocardial Infarction

At the time of publication of the Rand study there were no large RCTs to support or reject the use of CABG in the treatment of an acute MI. Patients with acute MI were excluded from CASS, VACS and ECSS. The issue of use of CABG in the treatment of acute MI is probably of diminishing importance. The introduction of thrombolytics and the use of PTCA in the treatment of an acute myocardial infarction makes unlikely the use of CABG as a primary treatment modality for a recent or evolving infarction unless coronary anatomy precludes the use of PTCA. We are aware of no large studies that look specifically at this question.

E. Following CABG

Rand found only "meager" research regarding CABG reoperation. Then extant studies confirmed clinicians' suspicions of higher mortality in patients undergoing reoperation. In these studies operative mortality ranged from 3-12 percent.

Despite the differences in operative mortality among men and women, analysis of long-term survival of surgical patients appears not to vary with gender. Eakers et al. (1989) found no difference in six-year survival between men and women in CASS. Similarly, as noted, Loop et al. (1983) found no significant differences based on gender in 10 year survival of patients undergoing surgery.

IV. FACTORS INFLUENCING THE CONCLUSIONS OF THE RAND STUDY

Changes in the practice of cardiology and cardiac surgery since the publication of studies reviewed by Rand and publication of their study have the potential to alter their indications for surgery. The introduction of thrombolytics, calcium channel blockers, improved beta-blockers and long-acting nitrates, PTCA, improvements in cardiac surgical techniques, and anesthetic technique all act to alter the outcomes associated with medical and surgical treatment of CAD.

The effects of the use of internal mammary artery (IMA) grafts in CABG will be discussed before considering the impact of PTCA on indications for CABG. Both of these modalities can have important effects on the use of CABG. Attention will focus predominantly on PTCA because of its role as an important invasive alternative to CABG. Abundant evidence exists to support the conclusion that PTCA has had an important effect on the characteristics of patients undergoing CABG (Califf et al. 1989, King and Talley 1989). Our focus on PTCA is not meant to diminish the potential importance of the other changes in medical and surgical practice on indications for CABG. Rather it reflects the fact that for many patients and classes of CAD, PTCA is a modality that is an important alternative to CABG.

A. Internal Mammary Artery Implantation

The use of the IMA in CABG has the potential for significant alteration in the long-term survival of patients undergoing CABG. Loop et al. (1986) reported 10 year survival among 2,306 patients who received IMA graft to the LAD was significantly better than among 3,625 patients who had only saphenous vein grafting. The extent of improvement ranged from 5 percent in patients with single-vessel disease (93.4 percent versus 88.0 percent, $P = 0.05$) to 11.5 percent in patients with double-vessel disease (90.0 percent versus 79.5 percent, $P < 0.0001$) and 11.6 percent in patients with triple-vessel disease (82.8 percent versus 71.0 percent, $P < 0.0001$). When adjusted for demographic and clinical differences, the data revealed that patients having only a vein graft had a risk of death during the first 10 years following surgery that was 1.61 times greater than patients receiving an IMA graft, a risk of late MI 1.21 times as great, a risk of reoperation 2.00 times as great, risk of late cardiac events 1.27 times as great and risk of cardiac rehospitalization that was 1.25 times as great.

Review of the CASS experience (Cameron et al. 1988) also revealed statistically significant improvements in 5 year survival among patients who received IMA grafts. IMA grafting reduced the risk of death by 64 percent. This advantage was found in all patient groups. Moreover, the study found that these long term survival advantages occurred without an increase in operative mortality, even in centers where the procedure was performed infrequently. These results led the authors to conclude that "IMA bypass graft is the graft of choice for CAD and should not be denied any subgroup of patients." It should be noted, however, that this study did not find statistically significant differences in the recurrence of anginal symptoms beyond three years following surgery.

The improved long-term survival with use of IMA suggests that the conclusions resulting from data in the VA, European and CASS studies about the lack of long-term survival benefits among patients undergoing CABG may not be applicable to patients undergoing CABG with IMA implantation. A significant survival advantage to CABG with IMA over medical treatment could require alteration in the accepted indications for CABG, especially in double vessel disease.

B. PTCA

Since its introduction by Dr. Andreas Greuntzig in 1977, PTCA has gained rapid acceptance for the treatment of selected groups of patients with CAD. As facility with the technique increased and designs of catheters improved, PTCA has been extended from being used simply for easily accessible single lesions in stable patients to treatment of more complex and multiple lesions in patients with multiple vessel disease and severe or unstable angina. Indeed, PTCA has changed the composition and outcome of the types of patients undergoing CABG today (Detre et al. 1988, Aricidi et al. 1988, Myler et al. 1987, King and Talley, 1989, Davie et al. 1989). Currently accepted indications for PTCA are presented in Table 1. Detailed indications for PTCA, from the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on PTCA) are presented in Appendix B.

In the sections that follow, results of selected clinical studies related to the efficacy of PTCA in the treatment of cardiac disease will be presented. Direct comparison of PTCA with CABG is limited by the lack of published results of RCTs that compare these two interventions. Studies currently underway should provide these comparisons.

TABLE 1

CURRENT INDICATIONS FOR CORONARY ANGIOPLASTY

Class I: Accepted Indications

Chronic stable angina unresponsive to medical therapy or unstable angina:

1. Preferably with objective evidence of myocardial ischemia
2. With good left ventricular function
3. With a single significant coronary stenosis suitable for PTCA

Class II: Evolving Indications

1. Chronic stable angina or unstable angina in patients with multivessel disease
2. Angina in patients with recent coronary occlusion (less than three months)
3. No angina or mild angina following medical therapy with a strongly positive exercise stress test
4. Documented variant angina with significant fixed lesions
5. Acute myocardial infarction
6. Angina after coronary bypass surgery
7. Angina in inoperable/high-risk patients
8. Angina in elderly patients ($\geq$ 75 years)

Class III: Relative Contraindications

1. No angina or mild angina without evidence of myocardial ischemia
2. Severe left ventricular dysfunction (ejection < 25%)
3. Significant left main coronary artery stenosis
4. Patients in whom the only lesions are chronic coronary occlusions (older than three months)

SOURCE: ISTF/WHO Guidelines for PTCA.

Caution is required in interpreting the results of early studies of PTCA. The experience of several investigators and the National Heart, Lung, and Blood Institute's (NHLBI) PTCA registry demonstrate a significant improvement in outcomes as operator and institutional experience in performing PTCA increases and as a result of improvements in catheter design (Talley et al. 1988, King and Talley 1989, Detre et al. 1988). Early studies probably understate the success rates of PTCA.

1. Chronic Stable Angina

Numerous clinical studies have demonstrated PTCA's ability to relieve anginal symptoms in patients with single and multiple vessel disease (Detre et al. 1988, Gruentzig et al. 1987, Faxon et al. 1984, Hirzel et al. 1984, Mabin et al. 1985, Myler et al, 1987 and others). The results of the NHLBI Registry are especially important because they reflect the results at several institutions and with large numbers of patients. The first registry (1977-1981) enrolled 3,248 patients from 105 clinical sites and the second registry (1985-1986) enrolled 1802 patients at 15 sites. This non-randomized study demonstrates the efficacy of PTCA in improving coronary blood flow and alleviating anginal symptoms. Angiographic success were 67 percent in the first registry and 88 percent in the second registry. Overall success rates (defined as a reduction of at least 20 percent in all lesions attempted, without death, MI or CABG) was 61 percent in the first registry and 78 percent in the second registry. Specific information on the relief of pain is not provided but, only 2.2 percent of patients in the new registry underwent elective CABG following PTCA (20.7 percent in first registry). These improvements occurred despite statistically significant increases in the proportion of patients with multivessel CAD, previous MI, previous CABG and poor left ventricular function. Mortality resulting from the procedure in both series was approximately 1 percent.

Outcomes of patients undergoing PTCA has been good. In follow-up of the 1977-1981 NHLBI registry patients, 72 percent of those who had initially successful procedures required no further procedures in the next year. 14 percent underwent repeat PTCA, 12 percent CABG, 5 percent experienced an MI and 1.6 percent died. At one year, two-thirds of patients were asymptomatic. Follow-up at 2 and 4 years was similar except few repeat PTCAs were required after the first year. Overall sustained improvements in symptoms occurred in 84 percent of patients who had an initially successful PTCA. (Kent et al. 1984).

Apparent success of PTCA at alleviating pain and improvements in operator expertise and catheter design has allowed for PTCA to be extended beyond the treatment of single type A lesions (see Table 2) in single vessel disease. King and Talley (1989) report the shifting pattern of PTCA use at Emory University Hospital over the period 1981 to 1986. They note that, in 1981, PTCA was performed as the initial revascularization procedure in 11 percent of patients undergoing revascularization while in 1986 44 percent underwent PTCA as the initial procedure (all other patients underwent CABG as their initial procedure). This shift was especially pronounced in single vessel disease which by 1986 had virtually ceased to be treated surgically in their institution.

These changes in patient populations are reflected in the second NHLBI PTCA Registry (1985-1986). Patients entered in the second registry were older, with more frequent left ventricular dysfunction, and more frequent histories of previous MI and CABG. Despite this more severe disease, the outcomes of patients entered in the second registry were superior to those of patients entered in the first registry. Angiographic success rates increased from 67 percent in the first registry to 88 percent ($p < 0.001$) in the second and overall success rates increased from 61 to 78 percent ($p. < 0.001$). In-hospital mortality

TABLE 2

CHARACTERISTICS OF LESIONS

Lesion-Specific Characteristics

Type A lesions (high success, > 85%; low risk)

- Discrete <10 mm length)
- Concentric
- Readily accessible
- Nonangulated segment, < 45°
- Smooth contour
- Little or no calcification
- Less than totally occlusive
- Not ostial in location
- No major branch involvement
- Absence of thrombus

Type B lesions (moderate success, 60-85%; moderate risk)*

- Tubular (10 to 20 mm length)
- Eccentric
- Moderate tortuosity of proximal segment
- Moderately angulated segment, > 45°, < 90°
- Irregular contour
- Moderate to heavy calcification
- Total occlusions < 3 months old
- Ostial in location
- Bifurcation lesions requiring double guide wires
- Some thrombus present

Type C lesions (low success, <60%; high risk)

- Diffuse (> 2 cm length)
- Excessive tortuosity of proximal segment
- Extremely angulated segments > 90°
- Total occlusion > 3 months old
- Inability to protect major side branches
- Degenerated vein grafts with friable lesions

* Although the risk of abrupt vessel closure is moderate, in certain instances the likelihood of a major complication may be low as in dilation of total occlusions < 3 months old or when abundant collateral channels supply the distalvessel.

SOURCE: ACC/AHA Task Force - Guidelines for PTCA.

among the second registry patients was one percent and the incidence of non-fatal MI was 4.3 percent (Detre et al., 1988). Follow-up at one-year confirms superior outcome among second registry patients (Detre et al. 1989).

As was the case for CABG, evidence that PTCA is effective at relieving angina does not necessarily mean that the procedure improves long-term mortality relative to medical treatment (or CABG). The longest follow-up of patients undergoing PTCA is from the initial series of 169 PTCAs performed by Gruentzig in the late 1970s. Cardiac survival was 96 percent at six years. (Gruentzig et al. 1987). Talley et al (1988) report similar findings among their series of 427 men who underwent PTCA during 1981 (98.1 percent cardiac survival).

It is difficult to generalize results based on these small early studies. Definitive resolution of the question of the effect of PTCA on long-term survival awaits the outcome of RCTs currently in progress. The extremely low incidence of operative mortality in patients with single and double vessel disease who undergo PTCA is as low as 0.07 percent in one study (Arcidi et al. 1988) makes this mortality comparison between PTCA and CABG more complex than it might initially appear.

The difficulty in comparing outcomes between modalities is seen in a review by Ellis et al. (1989) which compared PTCA with medical treatment of patients with single or double vessel disease with LAD involvement. This study compared 627 consecutive patients who underwent PTCA at Emory University Hospital in 1981-1983 with similar patient randomized to medical treatment in CASS (1975-1979). The study found no statistically significant difference overall. The data did reveal, however, that survival was improved in the subgroup of patients who underwent PTCA who had left ventricular dysfunction manifest by an EF less than 0.5 or

two vessel disease. Even these findings are subject to caveats since they reflect experience from different institutions at different times.

As noted previously, the current guidelines for use of PTCA in patients with stable angina are detailed in the ACC/AHA Task Force report that is presented in Appendix B.

2. Unstable Angina

PTCA has become a commonly used modality for the invasive treatment of unstable angina (UA). Indeed, almost half of the patients in the most recent NHLBI registry had unstable angina (versus 37 percent in the 1977-1981 group). As with single- and double-vessel disease generally, PTCA has been shown to be effective at relieving symptoms of unstable angina.

Comparison of data from the first NHLBI registry and CASS by Faxon et al. (1983) found that the in-hospital mortality and 18 month mortality and MI rates were similar in patients undergoing PTCA and CABG for UA. They found, however that improvement in angina was greater among patients undergoing PTCA than CABG (92 percent versus 80 percent). Caution must be taken in interpreting these data because of differences in the selection criteria and time periods of the two studies.

3. Acute Myocardial Infarction

The ACC/AHA Task Force guidelines endorse the use of PTCA in the presence of acute myocardial infarction (AMI) for the dilation of significant lesions in the infarct related

artery in patients; 1) in the low risk group for mortality and morbidity and with one or more Type A lesions and post-infarction angina evidence of severe myocardial ischemia during pre-discharge laboratory testing; or 2) recurrent episodes of ventricular tachycardia or ventricular fibrillation while on intensive antiarrhythmic therapy.

The ACC/AHA Task Force concluded that PTCA could be justified in patients who:

- are similar to patients mentioned above but have class B lesions, multivessel disease requiring PTCA, or are in the moderate risk for morbidity and/or mortality;
- are within the early hours of an evolving MI;
- have survived, or are within twelve hours of, the onset of cardiogenic shock;
- are asymptomatic but have a significant residual lesion in the infarct-related area after thrombolytic therapy;
- show objective evidence of myocardial ischemia during laboratory testing performed before discharge; and
- have had a non-Q wave MI and have single-vessel disease with type A lesions, and are on the low risk group for morbidity.

In all other patients the task force concluded that PTCA was not indicated in the setting of Acute MI.

4. Variant Angina

A study by Leisch et al (1986) demonstrates that PTCA can be effective in treating variant angina when there is a clinically significant fixed lesion associated with the vasospastic coronary arterial segment. This study was limited to only 22 patients and so it is difficult to generalize the results to a larger population.

5. Prior CABG

The high rate of morbidity and mortality associated with repeat CABG creates great interest in the use of PTCA as an alternative to surgery for patients with recurrence of symptoms due to progression of disease in native vessels or lesions in grafted saphenous veins or internal mammary arteries (IMAs). The limited data strongly suggests that PTCA is an appropriate first choice for revascularization of patients who have previously undergone CABG. A study of 116 patients with disabling angina pectoris following CABG was reported by Douglas et al. (1983). Successful reduction of angiographic stenosis occurred in 88 percent of patients. There were no deaths or neurologic complications in their patients. Follow-up (mean 8.3 months) found that 88 patients (76 percent) were free of angina or improved in their condition. Restenosis occurred in half the saphenous vein grafts and was especially common at the proximal graft anastomoses (53 percent).

Mortality related to surgical reoperation was reviewed by Douglas et al. (1983) as part of their assessment of the effectiveness of PTCA in treatment of patients with prior CABG. They note that Loop and his colleagues at the Cleveland Clinic in a report of 500 reoperations, experienced an operative mortality four times greater and a perioperative infarction rate three times greater in patients undergoing reoperation than in patients undergoing initial CABG (Loop et al, 1981).

F. Sudden Cardiac Death Survivors

The high rate of recurrence in patients who survive an episode of sudden cardiac death (SCD) has led to aggressive management of this group of patients. The few small studies reviewed by Rand failed to support the use of CABG to improve long-term survival in patients who survive SCD.

G. Ventricular Arrhythmias

The studies reviewed by Rand failed to demonstrate any improvement in survival among patients with ventricular arrhythmias who were randomized to CABG.

H. Variant Angina

We are aware of no RCT that have been performed to compare medical and surgical treatment of variant angina. A large study would be required because patients with variant angina constitute a diverse group. Many of them have coexisting fixed stenoses that are

responsible for significant reductions in coronary blood flow and many of them have co-existing disease in other vessels.

PTCA is a factor influencing the use of CABG in treatment of variant angina. A report by Leisch et al. (1986) documented the use of PTCA to treat this entity. They studied 22 patients with variant angina associated with fixed coronary stenoses of greater than 60 percent and found that 86 percent of these patients had a successful angioplasty (defined as a greater than 20% widening of the fixed stenosis). Restenoses occurred in 10 patients and repeat PTCA was required in 4 patients and CABG in 5 patients. This limited study, however, suggests a role for PTCA in treatment of variant angina and provides a basis for comparison with CABG.

I. Asymptomatic Patients

As defined by the Rand researchers, this group of patients is composed of those individuals with CAD that have yet to experience either angina or an MI. Their CAD is diagnosed as a result of an exercise stress test done as part of a "routine" evaluation, as, for example, in anticipation of the start of an exercise program. Angiography done subsequent to the positive stress test may reveal surgically correctable disease.

Data relating directly to this group of patients could not be identified. Rand suggests that data applicable to asymptomatic post MI patients is likely to apply to these patients. These data revealed no improvement in survival among patients treated surgically.

J. Groups underrepresented in RCTs

The elderly and women constitute two important groups underrepresented in the large trials. All three major RCTs specifically excluded patients over 65 from randomization. VACS and ECSS excluded women as well. If the findings of these studies cannot be generalized to the elderly and women, then their exclusions constitute a potentially critical limitation of the applicability of these studies to a Medicare demonstration.

1. The Elderly

Results reported by Gersh et al. (1985) suggest that CABG has an important role in the treatment of CAD in the elderly. They reviewed the outcomes of 1,491 patients (861 surgical, 630 medical) over age 65 who were entered into the CASS registry but were not randomized. These patients had mild (class I or II) angina as the primary surgical indication and at least one stenosis of more than 70%. The data revealed significantly greater survival among the surgical group (80% versus 63%, p. <0.0001). This advantage was not as pronounced among the oldest patients (age 75 or above) in whom 6 year survival was 75% in the surgical group and 56 percent in the medical group ($p = 0.044$). It should be noted that the small number of patients in this group (n - 78) is inadequate to detect small survival differences. The surgical group also had a significantly greater long-term alleviation of chest pain. Surgical benefits were greatest in patients with more severe CAD.

Two recent studies also address the question of the effects of age on outcome of CABG. Horneffer et al. (1987) reviewed outcomes of 228 consecutive patients age 70 or older who underwent CABG at the Johns Hopkins Hospital. This non-randomized study

matched these elderly patients with two prospective cohorts of patients of lesser age (one group age 55 to 69 and the other group less than 55 years old) who underwent CABG in the same time period. This study found significantly higher hospital mortality and morbidity among those over 70, but the researchers found this to reflect greater frequency of non-cardiac risk factors among these elderly patients. Late follow-up (77 +/- 19 months) failed to find any significant differences in survival or functional status based solely on age. Loop et al (1988) reviewed the outcome of 5,070 patients over the age of 65 who underwent CABG at the Cleveland Clinic between 1976 and 1986. Overall mortality in this group was 2.3 percent. Age over 75 and female gender were among the predictors of higher operative mortality. Perioperative morbidity was higher among older patients. Relief of angina was significantly higher among the elderly ($p=0.0001$) and longevity of those undergoing surgery exceeded actuarial predictions for the people of their age in the US population as a whole.

It is difficult to evaluate these non-randomized studies because of the potent effect that referral bias may have had on selection of patients undergoing surgery. This is likely to be especially significant among patients over age 75. These studies, however, seem to suggest that the benefits of CABG are applicable to the elderly and that advanced age, in and of itself, should not be a contraindication to CABG.

2. Women

Women are underrepresented in studies of CABG. Among the studies they reviewed, there was considerable diversity in the pre-operative clinical characteristics of women included in the studies. Not surprisingly, the conclusions drawn from these studies varied.

Some found superior anginal relief than experienced by men while others came to the opposite conclusion. The Rand group concluded that despite these conflicting reports:

> "there is evidence that [women] realize less symptom relief than men. Long-term survival data...suggest no substantial differences between the sexes.

Operative mortality rates for women undergoing CABG have been higher in most studies. Eaher et al (1989) found that to be the case in the eight studies they reviewed. The cause of this difference is uncertain. Fisher et al. (1982) reviewed CASS data and found that the greater mortality of women undergoing bypass was explained by their smaller size. Loop et al. (1983) found similar results when comparing Cleveland Clinic experience with 2,445 consecutive women undergoing CABG with that of 18,079 consecutive men. This was despite the fact that their female patients had significantly greater frequency of severe or unstable angina than the men (60 percent versus 45 percent, $p=0.0001$).

In contrast, a recent study by Khan et al. (1990) came to the opposite conclusions. Khan reviewed the experience of the Cedars-Sinai Medical Center with 2297 consecutive patients (21 percent women) undergoing CABG between 1982 and 1987. In-hospital mortality was significantly higher among women than men (4.6 percent versus 2.6 percent). Multivariate analysis of their data revealed that the increased mortality among women was a result of greater severity of disease among women referred for surgery. Correction for this eliminated differences in mortality. Body surface area was not found to be a statistically important variable. Khan concluded that the increased mortality rate among women was the result of referral bias.

APPENDIX A

INDICATIONS FOR CABG FROM THE 1984 CONSENSUS PANEL CONVENED BY THE RAND CORPORATION

APPENDIX A

INDICATIONS FOR CABG

Indication

ANGINA (type unspecified)

I. CABG indicated

- A. In patients with unacceptable symptoms during appropriate medical treatment
- B. In patients with progressive symptoms.

CHRONIC STABLE ANGINA

I. CABG Indicated

- A. Severity of pain
  1. In patients with chronic stable angina with unacceptable symptoms despite medical therapy.
- B. Arteriographic extent of disease
  1. In patients with significant left main stenosis.
  2. In patients with significant three-vessel disease.
  3. In patients with two-vessel disease, particularly if one of those lesions is in the proximal LAD.
  4. In patients with multiple coronary obstructions, good distal runoff, and normal or mildly altered left ventricular (LV) function.
- C. Miscellaneous
  1. In patients with chronic stable angina, even when they respond to medical management (especially patients in certain high-risk categories).

UNSTABLE ANGINA

I. CABG Indicated

- A. General considerations
  1. In patients with unstable angina after medical stabilization.
  2. Possibly indicated in patients with unstable angina.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication
3. Possibly indicated in patients with unstable angina during acute phase, refractory to medical management.
B. Severity of pain
1. In patients with unstable angina who do not respond to an intensive medical program.
2. In patients who have disabling unstable angina.
3. In patients suffering from unstable angina with intractable pain.
C. Type of pain
1. In patients with recurrent unstable angina.
2. In patients with the intermediate syndrome.
D. Arteriographic extent of disease
1. In patients with significant left main disease.
2. In patients with multivessel disease and relative preservation of LV function.
3. In patients with three- or possible two-vessel disease.
4. In patients with crescendo angina and severe three-vessel disease, left main disease, or proximal LAD disease.
VARIANT ANGINA
I. CABG Indicated
A. In patients with a fixed significant stenosis in addition to spasm.
B. In patients with a significant stenosis and disabling angina continuing despite optimal medical treatment.
C. Possibly indicated in patient with variant angina with a significant stenosis in addition to spasm.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication

II. CABG Not Indicated

A. In patients with variant angina who have no evidence of fixed obstructive lesions.

ASYMPTOMATIC PATIENTS

I. CABG Indicated

A. In asymptomatic patients with significant left main disease, three-vessel disease, or left main equivalent disease (proximal LAD and left circumflex).

II. CABG Not Indicated

A. In asymptomatic patients, there is no sound basis for recommending this procedure.

MYOCARDIAL INFARCTION

I. CABG Indicated

A. Symptoms
   1. In patients following (S/P) MI with angina.
   2. Possibly indicated in patients S/P MI with angina.

B. High-risk patient
   1. In "high-risk" patients S/P MI if coronary anatomy and LV function appropriate.
   2. Possibly indicated in high-risk post-MI patients who have positive exercise stress test at low work load.

C. In patients S/P MI if remaining coronary arteries have significant obstructive lesions.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication

D. Possibly indicated for complications of MI including ventricular aneurysm, VSD, mitral valve regurgitation.

II. CABG Not Indicated

A. In patients S/P MI as a routine procedure.

ACUTE MYOCARDIAL INFARCTION

I. CABG Indicated

A. Possibly indicated in patients with an acute MI less than a few hours in duration.

II. CABG Not Indicated

A. In patients with significant acute MI.

B. Relatively contraindicated in patients with an acute MI more than a few hours in duration unless there is some other surgical indication.

CONGESTIVE HEART FAILURE

I. CABG Indicated

A. Possibly indicated in patients with CHF and angina.

B. Possibly indicated in patients with severely depressed ventricular function and angina.

C. Possibly indicated in patients with CHF on the basis of potentially reversible ventricular dysfunction.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication

II. CABG Not Indicated

A. In patients with CHF.

B. In patients with CHF in the absence of severe angina.

C. In patients with CHF unless large ventricular aneurysm present or significant mitral insufficiency.

CARDIOGENIC SHOCK

I. CABG Indicated

A. Possibly indicated in patients with cardiogenic shock.

II. CABG Not Indicated

A. Usually not indicated in patients with cardiogenic shock S/P MI.

VENTRICULAR ARRHYTHMIAS

I. CABG Indicated

A. In patients with ventricular arrhythmias refractory to medical treatment.

B. In patients with runs of ventricular tachycardia associated with stress.

C. Possibly indicated for recurrent ventricular arrhythmias.

D. Possibly indicated in patients successfully resuscitated from sudden death.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication

E. CABG Not Indicated

F. In patients with arrhythmias

LEFT MAIN DISEASE

I. CABG Indicated

A. General considerations
1. In patients with significant left main disease.

B. Symptoms
1. In asymptomatic patients with left main disease.
2. In asymptomatic or symptomatic patients with significant left main disease, suitable distal vessels, and the absence of severe impairment of LV function.
3. In symptomatic patients with significant left main disease.
4. In patients with left main disease even though anginal symptoms are not disabling.

C. Degree of stenosis
1. In patients with high-grade left main obstruction
2. In patients with greater than 75% lesion of left main coronary artery.
3. In patients with greater than 50% lesion of left main artery, even when symptoms are slight.

THREE-VESSEL DISEASE

I. CABG Indicated

A. General considerations
1. In patients with obstruction of the three main coronary arteries.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication

2. Possibly indicated in patients with significant three-vessel disease.

B. Left ventricular function
   1. In patients with proximal three-vessel disease provided ventricular function is reasonably good.
   2. In patients with three-vessel disease and moderate impairment of LV function.

C. Symptoms
   1. In asymptomatic patients with three-vessel disease.
   2. In patients with three- and probably two-vessel disease when symptoms are absent or minimal as long as there is no severe impairment in LV function.
   3. In patients with severe obstruction of all three coronary arteries, even when symptoms are mild.
   4. In symptomatic patients with three-vessel disease.

LEFT ANTERIOR DESCENDING DISEASE

I. CABG Indicated

A. In asymptomatic patients with proximal LAD lesions or left main equivalent disease (proximal LAD and left circumflex).

B. In patients with LAD lesions accompanied by an obstruction of any other large remaining artery.

C. Possibly indicated in proximal LAD stenosis.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication

OTHER ANATOMIC LESIONS

I. CABG Indicated

A. In patients with severe (greater than or equal to 90%) lesion of any major artery that supplies a significant muscle mass regardless of symptoms.

II. CABG Not Indicated

A. Generally not indicated in patients with single-vessel disease other than in the presence of very proximal LAD lesions.

B. Generally not indicated in single-vessel disease unless symptoms cannot be managed adequately on medical treatment.

C. In patients with one-vessel disease and minimal or absent symptoms.

D. In patients unless constrictive lesion greater than 70% luminal diameter.

VALVULAR DISEASE

I. CABG Indicated

A. In patients undergoing surgery for valvular disease who have significant coronary arterial lesions.

B. In patients with aortic valvular disease associated with angina and significant coronary artery disease.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication

REOPERATION

I. CABG Indicated

A. May be indicated if incomplete revascularization is documented after first operation.

B. In symptomatic patients with bypassable lesions.

PROPHYLACTIC FOR OTHER SURGERY

I. CABG Not Indicated

A. In patients as prophylactic measure prior to other major surgery unless symptoms of angina are severe or there is other evidence of left main artery disease.

CONTRAINDICATIONS

I. CABG Not Indicated

A. Diffuse disease
   1. In patients with diffuse disease in the distal part of a stenotic artery.
   2. In patients with diffuse disease in all major and many secondary arteries and poor ventricular function.
   3. Relative contraindication in patients with inadequate coronary arterial runoff distal to a critical stenosis.

B. Ventricular function
   1. In patients with poor ventricular function.
   2. In patients with severe impairment of LV function.

APPENDIX A (Continued)

RAND INDICATIONS FOR CABG

Indication
3. Relative contraindications in severe nonreversible ventricular dysfunction.
C. In patients in order age groups.
D. Inpatients with concomitant, severe debilitating disease.

SOURCE: Indications for Selected Medical and Surgical Procedures- A Literature Review and Ratings of Appropriateness: Coronary Artery Bypass Graft Surgery, Rand Corporation, 1986.

APPENDIX B

GUIDELINES FOR PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY FROM THE AMERICAN COLLEGE OF CARDIOLOGY/ AMERICAN HEART ASSOCIATION TASK FORCE

2. the likelihood of abrupt vessel closure with subsequent morbidity and mortality, and
3. the likelihood of restenosis.

Although operator experience and individual patient characteristics are important factors relating to outcome, both procedural success and the development of abrupt vessel closure are largely determined by specific characteristics of the vessels and lesions involved. Recognizing the unique technical aspects of angioplasty and with the objective of fostering knowledgeable judgments about risk stratification, the Subcommittee has summarized three types of lesion-specific characteristics based on the current state of knowledge in Table I (see also section III-A).

Type A lesions have those characteristics that allow an anticipated success rate of ≥85% and have a low risk of abrupt vessel closure.

Type B lesions have those characteristics that result in a lower than optimal success rate ranging from 60 to 85% or have a moderate risk of abrupt vessel closure, or both.

Type C lesions have those characteristics that result in an unacceptably low success rate (<60%) or have a high risk of abrupt closure, or both.

It is recognized that we are dealing with a discipline of cardiovascular care that is undergoing considerable growth and development; as new insights are gained, we can anticipate further refinement of the guidelines for coronary angioplasty that are set forth in this document using the following classification:

Class I: Conditions for which there is general agreement that coronary angioplasty is justified. A class I indication should not be taken to mean that coronary angioplasty is the only acceptable therapy.

Class II: Conditions for which coronary angioplasty is performed but there is divergence of opinion with respect to its justification in terms of value and appropriateness.

Class III: Conditions for which there is general agreement that coronary angioplasty is not ordinarily indicated.

I. Single Vessel Coronary Artery Disease

A. Asymptomatic or Mildly Symptomatic (Functional class I) Patients With or Without Medical Therapy. Symptoms Are Defined in Accordance With the Canadian Cardiovascular Society Classification (Appendix C)

Class I

This category applies to patients who have a significant lesion* in a major epicardial artery that subtends a *large* area of viable myocardium and who

1. show evidence of *severe* myocardial ischemia while on medical therapy during laboratory testing, i.e., ischemia induced by *low level exercise* and manifested by
   a) ≥1 mm of ischemic ST segment depression in multiple leads, or
   b) reversible thallium perfusion defects in more than one vascular region, or
   c) exercise-induced reduction in the ejection fraction or wall motion abnormalities on radionuclide ventriculographic studies, or both, or
2. have been resuscitated from cardiac arrest or from sustained ventricular tachycardia in the absence of acute myocardial infarction, or
3. must undergo high risk noncardiac surgery, such as repair of an aortic aneurysm, iliofemoral bypass, or carotid artery surgery, if angina is present or there is objective evidence of ischemia, or
4. have a history of myocardial infarction together with a history of hypertension and ischemic ST segment depression on the baseline ECG.

All of these patients should

- have one or more type A lesions in the same vessel or its branches and
- be in the low risk group for morbidity (abrupt vessel closure <4%) and mortality (<0.5%).

Class II (mild or no symptoms, single vessel coronary disease)

This category applies to patients who have a significant lesion in a major epicardial artery that subtends at least a *moderate-sized* area of viable myocardium and who

1. show objective evidence of myocardial ischemia† while on medical therapy during laboratory testing, and
   a) have at least a moderate likelihood of successful dilation, and
   b) have a low risk of abrupt vessel closure, and
   c) are in the low risk group for morbidity and mortality.

Class III (mild or no symptoms, single vessel coronary disease)

This category applies to all other patients with single vessel disease and mild or no symptoms who do not fulfill the preceding criteria for class I or class II. It includes, for example, patients who

1. have only a small area of viable myocardium at risk, or
2. do not manifest evidence of myocardial ischemia during laboratory testing, or
3. have borderline lesions of <50% diameter reduction, or
4. have type C lesions, or

*For the purpose of this report, a significant stenosis is defined as one that results in a 50% reduction in coronary diameter as determined by caliper method.

†Evidence of myocardial ischemia during laboratory testing is taken to mean exercise-induced ischemia (with or without exercise-induced angina pectoris) manifested by ≥1 mm of ischemic ST segment depression or one or more exercise-induced reversible thallium perfusion defects and/or exercise-induced reduction in the ejection fraction and/or wall motion abnormalities on radionuclide ventriculographic studies.

5. are in the moderate or high risk group for morbidity and mortality.

Comments. In some patients, circumstances of occupation or employment may result in a class II indication being viewed as a class I category. Such patients would include individuals whose occupation involves the safety of others (airline pilots, bus drivers, truck drivers, air traffic controllers, for example) and those in certain occupations that frequently require sudden vigorous activity (fire fighters, police officers, athletes, for example). However, class III indications for asymptomatic or mildly symptomatic individuals with single vessel disease pertain to a risk profile that precludes the patient's suitability as a class I or II indication.

B. Symptomatic Patients With Angina Pectoris (functional classes II to IV, unstable angina) With Medical Therapy and Single Vessel Disease

Class I

This category applies to patients who have a significant lesion in a major epicardial artery that subtends at least a *moderate-sized* area of viable myocardium and who

1. show evidence of myocardial ischemia while on medical therapy during laboratory testing (including ECG monitoring at rest), or
2. have angina pectoris that has proved inadequately responsive to medical treatment. "Inadequately responsive" is taken to mean that patient and physician agree that angina significantly interferes with the patient's occupation or ability to perform his or her usual activities, or
3. are intolerant of medical therapy because of uncontrollable side effects.

All of these patients should

- have at least a moderate likelihood of successful dilation and
- be in the low risk group for morbidity and mortality.

Class II (symptomatic, single vessel coronary disease)

This category applies to patients who have a significant lesion in a major epicardial artery that subtends at least a *moderate-sized* area of viable myocardium and who

1. show evidence of myocardial ischemia while on medical therapy during laboratory testing (including ECG monitoring at rest) and
   a) have one or more type B lesions in the same vessel or its branches, or
   b) are in the moderate risk group for morbidity (abrupt vessel closure <8%) and mortality (<1%), or
2. have disabling symptoms and a *small* area of viable myocardium at risk, and
   a) at least a moderate likelihood of successful dilation, and
   b) are in the low risk group for morbidity and mortality, or
3. despite significant angina do not have objective evidence of myocardial ischemia while on medical therapy during laboratory testing, and
   a) have at least a moderate likelihood of successful dilation, and
   b) are in the low risk group for morbidity and mortality.

Class III (symptomatic, single vessel, coronary disease)

This category applies to all other symptomatic patients with single vessel disease who do not fulfill the preceding criteria for class I or class II. It includes, for example, patients who

1. have only a small area of viable myocardium at risk in the absence of disabling symptoms, or
2. have clinical symptoms not likely indicative of ischemia, or
3. have Type C lesions, or
4. are in the high risk group for morbidity and mortality.

Comments. Patients with single vessel disease who have significant symptoms constitute one of the largest groups of patients undergoing angioplasty. However, the generally excellent prognosis for patients with single vessel disease should be a paramount consideration before undertaking an interventional procedure in these patients. It is imperative that there be some assurance that the significant symptoms are indeed due to the coronary lesion proposed for dilation. Although significant symptoms may justify a lower tolerance for the risk of abrupt vessel closure or subsequent restenosis, one cannot compromise on the risk for significant mortality or morbidity.

II. Multivessel Coronary Artery Disease

A. Asymptomatic or Mildly Symptomatic (functional class I) Patients With or Without Medical Therapy

Class I

This category applies to patients who have one significant lesion in a major epicardial artery that could result in nearly complete revascularization because the additional lesion(s) subtends a small viable or nonviable area of myocardium. Additionally, patients in this category must

1. have a *large* area of viable myocardium at risk, and
2. show evidence of *severe* myocardial ischemia while on medical therapy during laboratory testing, or
3. have been resuscitated from cardiac arrest or from sustained ventricular tachycardia in the absence of acute myocardial infarction, or
4. be undergoing high risk noncardiac surgery and demonstrate objective evidence of ischemia, or
5. have a history of myocardial infarction together with a history of hypertension and ST segment depression on the baseline ECG.

All of these patients should
- have one or more type A lesions whose successful dilation would provide relief to all major regions of ischemia, and
- be in the low risk group for morbidity and mortality.

Class II (mild to no symptoms, multivessel coronary disease)

This category applies to patients who
1. are similar to patients in class I but who
   a) have a *moderate-sized* area of viable myocardium at risk, or
   b) have objective evidence of myocardial ischemia while on medical therapy, or
2. have significant lesions in two or more major epicardial arteries, each of which subtends at least a *moderate-sized* area of viable myocardium.

All of these patients should
- show evidence of myocardial ischemia while on medical therapy during laboratory testing, and
- have one or more type A or B lesions whose successful dilation would provide relief to all major regions of ischemia, and
- be in the low risk group for morbidity and mortality.

Class III (mild to no symptoms, multivessel disease)

This category applies to all other patients with multivessel disease and mild or no symptoms who do not fulfill the above criteria for class I or class II. It includes, for example, patients who
1. have only a small area of viable myocardium at risk, or
2. have a subtotally occluded vessel requiring angioplasty wherein the development of total occlusion of the vessel would result in severe hemodynamic collapse due to left ventricular dysfunction, or
3. have more than two major arteries with type B lesions, or
4. have type C lesions in major epicardial vessels serving moderate or large areas of viable myocardium, or
5. are in the moderate or high risk group for morbidity or mortality (for example, advanced left ventricular dysfunction [ejection fraction <20%] in the absence of angina or evidence of ischemia).

B. Symptomatic Patients With Angina Pectoris (functional classes II to IV, unstable angina) With Medical Therapy and Multivessel Disease

Class I

This category applies to patients who have significant lesions in each of two major epicardial arteries both subtending at least *moderate-sized* areas of viable myocardium and who:
1. show evidence of myocardial ischemia while on medical therapy during laboratory testing (including ECG monitoring at rest), or
2. have angina pectoris that has proved inadequately responsive to medical therapy, or
3. are intolerant of medical therapy because of uncontrollable side effects.

All of these patients should:
- have type A and B lesions whose successful dilation would provide relief of all major regions of ischemia, and
- be in the low risk group for morbidity and mortality.

Class II (symptomatic, multivessel disease)

This category applies to patients who have significant lesions in two or more major epicardial arteries that subtend at least *moderate-sized* areas of viable myocardium and who
1. are similar to patients in class I but who are in the moderate risk group for morbidity and mortality, or
2. have angina pectoris but do not necessarily have objective evidence of myocardial ischemia while on medical therapy during laboratory testing.

All of these patients should
- have type A and B lesions whose successful dilation would provide relief of all major regions of ischemia, and
- be in the moderate risk group for morbidity and mortality
3. have disabling angina that has proved inadequately responsive to medical therapy, and
   a) be considered a poor candidate for surgery because of advanced physiologic age or coexisting medical disorders, and
   b) have one or more type A and B lesions that cannot be successfully dilated, and
   c) be in the moderate risk group for morbidity and mortality.

Class III (symptomatic, multivessel coronary disease)

This category applies to all other symptomatic patients with multivessel disease who do not fulfill the preceding criteria in class I or class II. It includes, for example, patients who
1. have only a small area of myocardium at risk in the absence of disabling symptoms, or
2. have a subtotally occluded vessel requiring angioplasty wherein the development of total occlusion of the vessel would result in severe hemodynamic collapse due to left ventricular dysfunction, or
3. have type C lesions in major epicardial vessels serving moderate or large areas of viable myocardium, or
4. are in the high risk group for morbidity or mortality, or both.

Comments. It is to be stressed that risk assessment is different in patients with multivessel as compared

with single vessel disease. In the former there ideally should be the opportunity for anatomically complete revascularization, although it is recognized that adequate functional revascularization can be achieved without necessarily being anatomically complete. In every instance the goal is to achieve relief of ischemia at a risk acceptable for the procedure. In estimating this risk in multivessel disease it is imperative that each lesion be considered in the context of all other lesions present. Some assessment must then be made of the consequences likely to ensue should any one of the attempted dilations fail and result in abrupt vessel closure. For example, it would be judged inappropriate to attempt dilation of a proximal high grade left anterior descending artery lesion if that vessel was supplying many collateral vessels to a large area of viable myocardium in the distribution of a totally occluded dominant right coronary artery.

III. Acute Myocardial Infarction (Angioplasty During Initial Hospitalization)

Class I

This category applies to the dilation of a significant lesion, in the infarct-related artery only, in patients who

1. have recurrent episodes of ischemic chest pain particularly if accompanied by ECG changes (postinfarction angina), or
2. show evidence of *severe* myocardial ischemia while on medical therapy during laboratory testing performed before hospital discharge, or
3. have recurrent ventricular tachycardia or ventricular fibrillation, or both, while on intensive antiarrythmic therapy.

All of these patients should:

- have one or more type A lesions and
- be in the low risk group for morbidity and mortality.

Class II

This category applies to the dilation of significant lesions in patients who

1. are similar to patients in class I but who
   a) have type B lesions, or
   b) undergo multivessel angioplasty, or
   c) are in the moderate risk group for morbidity or mortality, or both, or
2. are within the very early hours of an evolving myocardial infarction, with or without thrombolytic therapy, or
3. are within 12 hours of the onset of cardiogenic shock or, in those who have survived cardiogenic shock, in the period before discharge, or
4. are asymptomatic and have a significant residual lesion in the infarct-related artery after thrombolytic therapy, or
5. show objective evidence of myocardial ischemia during laboratory testing performed before discharge, or
6. have had a non-Q wave myocardial infarction, and
   a) have single vessel disease with
   b) type A lesions, and
   c) are in the low risk group for morbidity and mortality.

Class III

This category applies to all other patients in the immediate postinfarction period (during initial hospitalization) who do not fulfill the preceding criteria for class I and class II. For example:

1. undertaking dilation of additional lesions in a vessel other than the infarct related artery within the early hours of infarction (0 to 6 hours), or
2. dilation of residual lesions that are borderline (50 to 60% diameter reduction), or
3. dilation of type C lesions, or
4. undertaking angioplasty in patients in the high risk group for morbidity and mortality.

Comments. The role of angioplasty in the management of patients during the course of an acute myocardial infarction is currently the subject of intense investigation. Although there is evidence that the procedure can be used effectively as a primary means of establishing reperfusion in the very early hours of an evolving infarction,[41,42] many important questions remain unresolved, such as the impact of procedural delay required to undertake angioplasty, the influence of thrombus on abrupt vessel closure and subsequent restenosis.

The use of angioplasty in conjunction with thrombolytic therapy is of particular interest and is thought by many to hold great promise. A note of caution is warranted, however, in light of the findings of three separate large randomized trials[43–45] that have recently reported adverse effects when angioplasty was performed immediately, rather than later, after the administration of tissue plasminogen activator. The optimal timing and long-term benefit of angioplasty in the management of patients with acute infarction are questions that must await further data.

Appendix A
Training and Credentialing

It is generally acknowledged that specialized skills are required for coronary interventional techniques. Training in these procedures necessitates thorough skills in diagnostic and therapeutic cardiology and particularly cardiac catheterization and angiography. Whereas the majority of individuals currently performing angioplasty learned the technique by observing experts and attending "how-to" seminars, the complexity of the procedure and the recognized need for hands-on experience dictate that formal training programs in angioplasty become the required means of learning. Entrance requirements to such programs should follow the completion of a structured cardiology fellowship training

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